Commissioner to charge any fees due to Arnold, White & Durkee Deposit Acct. No. 01-2508/CADL:002/PAR.

REMARKS

I. Status of the Claims

Claims 19 and 62-65 are pending in the application. In a paper filed concurrent herewith, applicants are requesting for entry of amendments previously denied entry by the examiner, along with entry of new claims 66-79. This "transitional after final" practice is proper in this case given the priority date of November 3, 1988. Applicants seek to provide the following remarks prior to the examiner's issuance of an action in order to expedite the prosecution.

II. Rejection Under § 112, First Paragraph

The examiner has maintained the rejection of claims 19 and 65 under § 112, first paragraph on the grounds that the specification does not provide any evidence that administration of UTAA will "enhance" the production of antibodies. In the previous response, applicants respectfully traversed the rejection, pointing out that claims 19 and 65 were supported by the specification in both diagnostic and therapeutic contexts and, further, pointed out that the examiner had failed to advance any scientific reasoning against the operability of these claims with respect to either of these endeavors.

In fact, the specification contains more than enough disclosure regarding enhancement of antibody production to support claims 19 and 65. As described in the Background, many melanoma

patients have antibodies against UTAA. Page 7, lines 25-33. In such patients, further administration of purified UTAA would be expected to stimulate the production of antibodies, and the examiner has offered no reason why this would not be the case. Finally, in a declaration from one of the inventors, Dr. Rishab Gupta, the antibody titers of four melanoma patients are shown following administration of UTAA in the form of a mixed cell vaccine. In each case, the anti-UTAA titers rose significantly following administration.

The examiner has refuted the declaratory showing on the grounds that the data were generated using whole cells and not purified antigen. While true, the relevance of this distinction is unclear; in effect, why would those of skill in the art believe that the ability to enhance antibody production to UTAA using a cell membrane-bound form of the antigen would not also indicate that free UTAA could enhance antibody production? Applicants submit that there is no reason to question the ability of free UTAA to act as the cell membrane-bound form does. In fact, it has been shown that free UTAA is a potent antigen in the baboon system. Hunt *et al.*, *Cancer Immunol. Immunother.* 34:377-382 (1992). The examiner failed to address these points in the Advisory Action and an explanation of why these comments are not sufficient to overcome the rejection is requested.

III. Rejection over Real

Claims 19 and 62 are rejected under § 102(b) as allegedly anticipated by Real *et al.* (U.S. Patent 4,562,160; "Real"). Real is said to disclose an antigen composition comprised of a tumor

associated antigen having a molecular weight of 90-100 kD which is useful for antibody production. The examiner argues that UTAA may be Real's antigen, designated "FD."

Applicants have provided a variety of reasons why the Real antigen cannot be UTAA. First, applicants have noted that there appears to be a considerable size difference between UTAA and FD under non-reducing conditions. Second, the tissue distribution of FD is much smaller than UTAA in melanoma patients. And third, applicants have provided a table listing further distinguishing characteristics of UTAA and FD.

The examiner's only response to these submissions is to argue that the table contains properties that are not "claim limitations" and, hence, applicants are not entitled to rely on those distinctions. This is incorrect as a matter of law. The rejected claims recite UTAA, and UTAA has the properties listed in the table of the last response. There is no basis for arguing that each and every characteristic of UTAA needs to be recited in the claims. Rather, the specification defines UTAA both physically and immunologically; the properties of the antigen thus defined are relevant to its identity regardless of whether they are actually recited in the claim.

In the interest of advancing the prosecution, applicants have provided a series of new claims that incorporate a variety of different recitations. Each of these recitations presents separate points of patentability with respect to the Real patent. The examiner's careful evaluation of each claim is respectfully requested.

IV. Rejection Over Euhus

Claims 19 and 62-64 are again rejected as anticipated or rendered obvious by Euhus *et al.* ("Euhus"). According to the examiner, Euhus discloses a 110 kD version of UTAA that appears to be the same antigen as that claimed, or at least an obvious variation thereof. In addition, Euhus is said to disclose the production of antibodies, implying the administration of the antigen to an animal for the purpose of eliciting UTAA-reactive antibodies. Applicants respectfully traverse the rejection.

Applicants again note that the Euhus abstract is not enabling for the production of UTAA. It is well established that a reference must teach how to make and use, *i.e.*, must enable the claimed invention for it to be a valid reference against the claims of an application. In *Paperless Accounting Inc. v. Bay Area Rapid Transit Sys.*, 231 U.S.P.Q. 649 (Fed. Cir. 1986), the PTO's reviewing court said that a "§ 102(b) reference 'must sufficiently describe the claimed invention to have placed the public in possession of it'.... '[E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling.'"

Turning to the abstract, it is true that an antibody specific for UTAA is disclosed and that a purified form of UTAA is described. None of the foregoing is relevant, however, to the question of anticipation (or obviousness) of an invention relating to an antigen composition or methods of immunization. Merely disclosing "an antibody for UTAA" or various separative techniques does not provide an enabling disclosure for the production of an antigen composition according to the present invention, and thus does not place the invention in the hands of the public, as required under §102.

This view is supported by the declaration of Dr. Ralph Reisfeld, Head of the Department of Molecular Immunology at the Scripps Institute. Dr. Reisfeld stated that the Euhus abstract would not be enabling for UTAA or for methods relating to the diagnosis of melanoma using UTAA or UTAA-specific antibodies. In particular, "key conditions such as the proper pH or ionic strength under which isolation was conducted are missing, as are the migration distances or retention times for gel or column purification." According to Dr. Reisfeld, the absence of these details prevents the reproducible isolation and purification of UTAA.

In response, the examiner has substituted her view that the Euhus abstract would provide sufficient teachings. This is improper - the examiner cannot refute a declaratory submission from a qualified expert simply of the grounds of personal disbelief. If the examiner has some basis for believing Dr. Reisfeld is not qualified or that Dr. Reisfeld's declaration is without scientific foundation, let the examiner file an affidavit to place those concerns on the record.

The maintenance of the rejection is further improper in that the examiner attempts to rely on the specification to show the ease with which various separation procedures could be employed. This ignores (i) the case law which precludes applicants' specification from being used against their own claims and (ii) the additional disclosure provided by the specification, not found in the abstract, that breathes meaning and significance into the excerpted passage. In short, the instant application, which is not prior art, is enabling, whereas the abstract is not enabling; these facts do not support a rejection of the former over the latter.

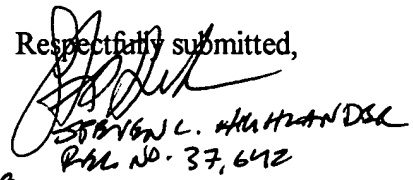
The examiner also has ignored the separate patentability of claims 63, 64 and 65. Recitations in these claims cannot not be found in the abstract, enabled by the abstract, or even suggested by the abstract. The examiner has not addressed the merits of these claims; consideration is respectfully requested.

Finally, it is noted that a variety of new claims have been proposed that offer separate grounds for patentability over Euhus. Examination thereof is respectfully requested.

VI. Summary

In light of the foregoing amendments and remarks, applicants submit that all claims are in condition for allowance and solicit an early indication to that effect. Should Examiner Sidberry feel that further discussion of any remaining issues would advance the prosecution, she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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